

60/139,070, filed June 11, 1999 and United States  
provisional application 60/190,211, filed March 17, 2000.

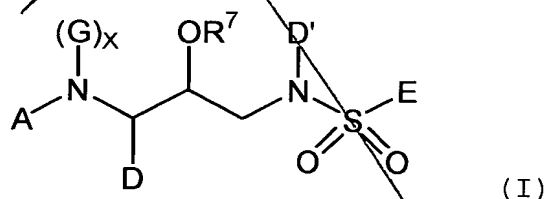
IN THE CLAIMS

Please cancel, without prejudice, claim 6.

Please amend claims 1-4, 8-9, 11, 15-18 and 21-22

as follows:\*

1. (Amended) A compound of the formula (I):



and pharmaceutically acceptable salts thereof; wherein:

A is tetrahydrofurodihydrofuranyl-O-C(O)-, wherein tetrahydrofurodihydrofuranyl is optionally substituted with one or more substituents independently selected from oxo, -OR<sup>2</sup>, SR<sup>2</sup>, -R<sup>2</sup>, -N(R<sup>2</sup>)(R<sup>2</sup>), -R<sup>2</sup>-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -N(R<sup>2</sup>)-C(O)O-R<sup>2</sup>, -C(O)-R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>, -S(O)<sub>n</sub>-Q, methylenedioxy, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, -NO<sub>2</sub>, Q, -OQ, -OR<sup>7</sup>, -SR<sup>7</sup>, -R<sup>7</sup>, -N(R<sup>2</sup>)(R<sup>7</sup>) or -N(R<sup>7</sup>)<sub>2</sub>;

\* An "Appendix of Amendments" is enclosed at Tab A, showing the amendments to claims 1-4, 8-9, 11, 15-18 and 21-

each Ht is independently selected from C<sub>3</sub>-C<sub>7</sub> cycloalkyl; C<sub>5</sub>-C<sub>7</sub> cycloalkenyl; C<sub>6</sub>-C<sub>14</sub> aryl; or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, N(R<sup>2</sup>), O, S and S(O)<sub>n</sub>; wherein said aryl or said heterocycle is optionally fused to Q; and wherein any member of said Ht is optionally substituted with one or more substituents independently selected from oxo, -OR<sup>2</sup>, SR<sup>2</sup>, -R<sup>2</sup>, -N(R<sup>2</sup>)(R<sup>2</sup>), -R<sup>2</sup>-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -N(R<sup>2</sup>)-C(O)O-R<sup>2</sup>, -C(O)-R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>, -S(O)<sub>n</sub>-Q, methylenedioxy, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, -NO<sub>2</sub>, Q, -OQ, -OR<sup>7</sup>, -SR<sup>7</sup>, -R<sup>7</sup>, -N(R<sup>2</sup>)(R<sup>7</sup>) or -N(R<sup>7</sup>)<sub>2</sub>;

each R<sup>2</sup> is independently selected from H, or C<sub>1</sub>-C<sub>4</sub> alkyl optionally substituted with a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, S, S(O)<sub>n</sub> or N(R<sup>33</sup>); wherein any of said ring systems or N(R<sup>33</sup>) is optionally substituted with 1 to 4 substituents independently selected from -X'-Y', -O-arylalkyl, -S-arylalkyl, -N(Y')<sub>2</sub>, -N(H)-arylalkyl, -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-arylalkyl, oxo, -O-(C<sub>1</sub>-C<sub>4</sub> alkyl), OH, C<sub>1</sub>-C<sub>4</sub>

22. In the Appendix, the added portion is underscored and the deleted portion is bracketed.

alkyl, -SO<sub>2</sub>H, -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>-NH<sub>2</sub>, -SO<sub>2</sub>-NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>-N(C<sub>1</sub>-C<sub>4</sub> alkyl)<sub>2</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)<sub>2</sub>, -NH-C(O)H, -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-C(O)H, -NH-C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, -C<sub>1</sub>-C<sub>4</sub> alkyl-OH, -OH, -CN, -C(O)OH, -C(O)O-C<sub>1</sub>-C<sub>4</sub> alkyl, -C(O)-NH<sub>2</sub>, -C(O)-NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(O)-N(C<sub>1</sub>-C<sub>4</sub> alkyl)<sub>2</sub>, halo or -CF<sub>3</sub>;

X' is -O-, -S-, -NH-, -NHC(O)-, -NHC(O)O-, -NHSO<sub>2</sub>-, or -N-(C<sub>1</sub>-C<sub>4</sub>)alkyl-;

Y' is C<sub>1</sub>-C<sub>15</sub> alkyl, C<sub>2</sub>-C<sub>15</sub> alkenyl or alkynyl, wherein one to five carbon atoms in Y' are optionally substituted with C<sub>3</sub>-C<sub>7</sub> cycloalkyl or C<sub>5</sub>-C<sub>6</sub> cycloalkenyl, C<sub>6</sub>-C<sub>14</sub> aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, NH, O, S and S(O)<sub>n</sub>;

each R<sup>3</sup> is independently selected from H, Ht, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl or C<sub>5</sub>-C<sub>6</sub> cycloalkenyl; wherein any member of said R<sup>3</sup>, except H, is optionally substituted with one or more substituents selected from -OR<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O)<sub>n</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)O(R<sup>2</sup>), -N(R<sup>2</sup>)-C(O)N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, Ht, -CN, -SR<sup>2</sup>, -C(O)OR<sup>2</sup>, or N(R<sup>2</sup>)-C(O)-R<sup>2</sup>;

each R<sup>33</sup> is selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl or C<sub>5</sub>-C<sub>6</sub> cycloalkenyl, C<sub>6</sub>-C<sub>14</sub> aryl or a 5-7 membered saturated or

unsaturated heterocycle, containing one or more heteroatoms selected from N, NH, O, S and S(O)<sub>n</sub>;

each n is independently 1 or 2;

G is selected from H, R<sup>7</sup> or C<sub>1</sub>-C<sub>4</sub> alkyl;

x in (G)<sub>x</sub> is 1;

D is C<sub>1</sub>-C<sub>6</sub> alkyl substituted with Q, wherein said alkyl is optionally substituted with one or more groups selected from C<sub>3</sub>-C<sub>6</sub> cycloalkyl, -R<sup>3</sup>, -O-Q or Q;

each Q is independently selected from a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; wherein Q contains one substituent selected from -OR<sup>2</sup>, -OR<sup>8</sup>, -O-arylalkyl, -SR<sup>8</sup>, -S-arylalkyl, -N(R<sup>2</sup>)R<sup>8</sup>, -N(R<sup>2</sup>)-arylalkyl and may be optionally substituted with one or more additional substituents independently selected from oxo, -OR<sup>8</sup>, -O-arylalkyl, -SR<sup>8</sup>, -S-arylalkyl, -N(R<sup>2</sup>)R<sup>8</sup>, -N(R<sup>2</sup>)-arylalkyl, -OR<sup>2</sup>, -R<sup>2</sup>, -SO<sub>2</sub>R<sup>2</sup>, -SO<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -OH, (C<sub>1</sub>-C<sub>4</sub>)-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, halo or -CF<sub>3</sub>;

each R<sup>8</sup> is independently selected from Ht', -C<sub>1</sub>-C<sub>15</sub> branched or straight chain alkyl, alkenyl or alkynyl wherein one to five carbon atoms in said alkyl, alkenyl or alkynyl are independently replaced by W, or wherein one to five carbon atoms in said alkyl, alkenyl or alkynyl are substituted with Ht'; and wherein R<sup>8</sup> is additionally and

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optionally substituted with one or more groups independently selected from -OH; -S(C<sub>1</sub>-C<sub>6</sub> alkyl); -CN; -CF<sub>3</sub>; -N(R<sup>2</sup>)<sub>2</sub>; halo; -C<sub>1</sub>-C<sub>4</sub>-alkyl; -C<sub>1</sub>-C<sub>4</sub>-alkoxy; -Ht'; -O-Ht'; -NR<sup>2</sup>-CO-N(R<sup>2</sup>)<sub>2</sub>; -CO-N(R<sup>2</sup>)<sub>2</sub>; -R<sup>1</sup>-C<sub>2</sub>-C<sub>6</sub> alkenyl, which is optionally substituted with one or more groups independently selected from hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, -Ht', -O-Ht', -NR<sup>2</sup>-CO-N(R<sup>2</sup>)<sub>2</sub> or -CO-N(R<sup>2</sup>)<sub>2</sub>; or R<sup>7</sup>;

wherein W is -O-, -NR<sup>2</sup>-, -S-, -C(O)-, -C(S)-, -C(=NR<sup>2</sup>)-, -S(O)<sub>2</sub>-, -NR<sup>2</sup>-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-NR<sup>2</sup>-, -NR<sup>2</sup>-C(O)O-, -O-C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-C(S)NR<sup>2</sup>-, -CONR<sup>2</sup>-, -NR<sup>2</sup>C(O)-, -C(S)NR<sup>2</sup>-, -NR<sup>2</sup>C(S)-, -NR<sup>2</sup>-C(=N-CN)-NR<sup>2</sup>-, -NR<sup>2</sup>C(=N-CN)O- or -C(O)O-;

each Ht' is independently selected from C<sub>3</sub>-C<sub>7</sub> cycloalkyl; C<sub>5</sub>-C<sub>7</sub> cycloalkenyl; C<sub>6</sub>-C<sub>14</sub> aryl; 5-7 membered saturated or unsaturated heterocycle containing one or more heteroatoms selected from N, N(R<sup>2</sup>), O, S and S(O)<sub>n</sub>; wherein said aryl or said heterocycle is optionally fused to Q'; and wherein any member of said Ht' is optionally substituted with one or more substituents independently selected from oxo, -OR<sup>2</sup>, SR<sup>2</sup>, -R<sup>2</sup>, -N(R<sup>2</sup>)(R<sup>2</sup>), -R<sup>2</sup>-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -N(R<sup>2</sup>)-C(O)O-R<sup>2</sup>, -C(O)-R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>, -S(O)<sub>n</sub>-Q', methylenedioxy, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, -NO<sub>2</sub>, Q', -OQ', -OR<sup>7</sup>, -SR<sup>7</sup>, -R<sup>7</sup>, -N(R<sup>2</sup>)(R<sup>7</sup>) or -N(R<sup>7</sup>)<sub>2</sub>;

each Q' is independently selected from a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, S, S(O)<sub>n</sub> or N(R<sup>2</sup>);

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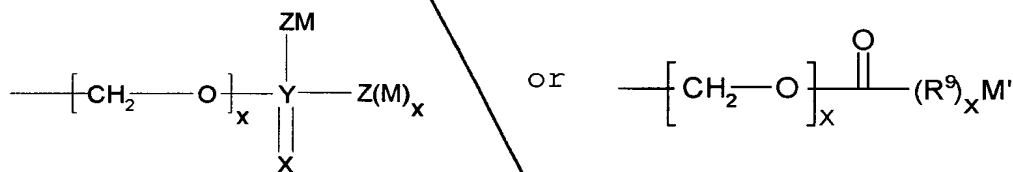
D' is selected from C<sub>1</sub>-C<sub>15</sub> alkyl, C<sub>1</sub>-C<sub>15</sub> alkoxy, C<sub>2</sub>-C<sub>15</sub> alkenyl, C<sub>2</sub>-C<sub>15</sub> alkenyloxy, C<sub>2</sub>-C<sub>15</sub> alkynyl, or C<sub>2</sub>-C<sub>15</sub> alkynyloxy, wherein D' optionally comprises one or more substituents independently selected from Ht, oxo, halo, -CF<sub>3</sub>, -OCF<sub>3</sub>, -NO<sub>2</sub>, azido, -SH, -SR<sup>3</sup>, -N(R<sup>3</sup>)-N(R<sup>3</sup>)<sub>2</sub>, -O-N(R<sup>3</sup>)<sub>2</sub>, -(R<sup>3</sup>)N-O-(R<sup>3</sup>), -N(R<sup>3</sup>)<sub>2</sub>, -CN, -CO<sub>2</sub>R<sup>3</sup>, -C(O)-N(R<sup>3</sup>)<sub>2</sub>, -S(O)<sub>n</sub>-N(R<sup>3</sup>)<sub>2</sub>, -N(R<sup>3</sup>)-C(O)-R<sup>3</sup>, -N(R<sup>3</sup>)-C(O)-N(R<sup>3</sup>)<sub>2</sub>, -C(O)-R<sup>3</sup>, -S(O)<sub>n</sub>-R<sup>3</sup>, -N(R<sup>3</sup>)-S(O)<sub>n</sub>(R<sup>3</sup>), -N(R<sup>3</sup>)-S(O)<sub>n</sub>-N(R<sup>3</sup>)<sub>2</sub>, -S-NR<sup>3</sup>-C(O)R<sup>3</sup>, -C(S)N(R<sup>3</sup>)<sub>2</sub>, -C(S)R<sup>3</sup>, -NR<sup>3</sup>-C(O)OR<sup>3</sup>, -O-C(O)OR<sup>3</sup>, -O-C(O)N(R<sup>3</sup>)<sub>2</sub>, -NR<sup>3</sup>-C(S)R<sup>3</sup>, =N-OH, =N-OR<sup>3</sup>, =N-N(R<sup>3</sup>)<sub>2</sub>, =NR<sup>3</sup>, =NNR<sup>3</sup>C(O)N(R<sup>3</sup>)<sub>2</sub>, =NNR<sup>3</sup>C(O)OR<sup>3</sup>, =NNR<sup>3</sup>S(O)<sub>n</sub>-N(R<sup>3</sup>)<sub>2</sub>, -NR<sup>3</sup>-C(S)OR<sup>3</sup>, -NR<sup>3</sup>-C(S)N(R<sup>3</sup>)<sub>2</sub>, -NR<sup>3</sup>-C[=N(R<sup>3</sup>)]-N(R<sup>3</sup>)<sub>2</sub>, -N(R<sup>3</sup>)-C[=N-NO<sub>2</sub>]-N(R<sup>3</sup>)<sub>2</sub>, -N(R<sup>3</sup>)-C[=N-NO<sub>2</sub>]-OR<sup>3</sup>, -OC(O)R<sup>3</sup>, -OC(S)R<sup>3</sup>, -OC(O)N(R<sup>3</sup>)<sub>2</sub>, -C(O)N(R<sup>3</sup>)-N(R<sup>3</sup>)<sub>2</sub>, -N(R<sup>3</sup>)-N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)-OC(O)R<sup>3</sup>, -N(R<sup>3</sup>)-OC(O)R<sup>3</sup>, -N(R<sup>3</sup>)-OC(O)R<sup>3</sup>, -OC(S)N(R<sup>3</sup>)<sub>2</sub>, -OC(S)N(R<sup>3</sup>)(R<sup>3</sup>), or -PO<sub>3</sub>-R<sup>3</sup>;

E is selected from Ht; Ht-Ht; Ht fused with Ht; -O-R<sup>3</sup>; -N(R<sup>2</sup>)(R<sup>3</sup>); C<sub>1</sub>-C<sub>6</sub> alkyl, which is optionally

substituted with one or more groups selected from  $R^4$  or Ht;  
 $C_2-C_6$  alkenyl, which is optionally substituted with one or  
more groups selected from  $R^4$  or Ht;  $C_3-C_6$  saturated  
carbocycle, which is optionally substituted with one or more  
groups selected from  $R^4$  or Ht; or  $C_5-C_6$  unsaturated  
carbocycle, which is optionally substituted with one or more  
groups selected from  $R^4$  or Ht;

each  $R^4$  is independently selected from  $-R^2$ ,  $-OR^2$ ,  
 $-OR^3$ ,  $-SR^2$ ,  $-SOR^2$ ,  $-SO_2R^2$ ,  $-CO_2R^2$ ,  $-OC(O)-R^2$ ,  $-C(O)-N(R^2)_2$ ,  
 $-C(O)-NR^2(OR^2)$ ,  $-S(O)_2-N(R^2)_2$ , halo,  $-NR^2-C(O)-R^2$ ,  $-NR^2-OR^2$ ,  
 $-N(R^2)_2$  or  $-CN$ ;

each  $R^7$  is independently selected from hydrogen,



wherein each M is independently selected  
from H, Li, Na, K, Mg, Ca, Ba,  $-N(R^2)_4$ ,  $C_1-C_{12}$ -alkyl,  
 $C_2-C_{12}$ -alkenyl, or  $-R^6$ ; wherein 1 to 4  $-CH_2$  radicals of the  
alkyl or alkenyl group, other than the  $-CH_2$  that is bound to  
Z, is optionally replaced by a heteroatom group selected  
from O, S,  $S(O)$ ,  $S(O_2)$ , or  $N(R^2)$ ; and wherein any hydrogen  
in said alkyl, alkenyl or  $R^6$  is optionally replaced with a  
substituent selected from oxo,  $-C_1-C_4$  alkyl,  $-N(R^2)_2$ ,  $-N(R^2)_3$ ,

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~~-OH, -O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -CN, -C(O)OR<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>,  
S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sub>2</sub>, C(O)R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>,  
-S(O)<sub>n</sub>-R<sup>6</sup>, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, or -NO<sub>2</sub>;~~

~~M' is H, C<sub>1</sub>-C<sub>12</sub>-alkyl, C<sub>2</sub>-C<sub>12</sub>-alkenyl, or -R<sup>6</sup>;~~

~~wherein 1 to 4 -CH<sub>2</sub> radicals of the alkyl or alkenyl group  
is optionally replaced by a heteroatom group selected from  
O, S, S(O), S(O<sub>2</sub>), or N(R<sup>2</sup>); and wherein any hydrogen in  
said alkyl, alkenyl or R<sup>6</sup> is optionally replaced with a  
substituent selected from oxo, -OR<sup>2</sup>, -C<sub>1</sub>-C<sub>4</sub> alkyl, -N(R<sup>2</sup>)<sub>2</sub>,  
N(R<sup>2</sup>)<sub>3</sub>, -OH, -O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -CN, -C(O)OR<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>,  
-S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sub>2</sub>, -C(O)R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>,  
-S(O)<sub>n</sub>-R<sup>6</sup>, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, or -NO<sub>2</sub>;~~

~~x, when associated with R<sup>7</sup>, is 0 or 1;~~

~~Z is O, S, N(R<sup>2</sup>)<sub>2</sub>, or, when M is not present, H;~~

~~Y is P or S;~~

~~X is O or S;~~

~~R<sup>9</sup> is C(R<sup>2</sup>)<sub>2</sub>, O or N(R<sup>2</sup>); wherein when Y is S, Z is  
not S; and~~

~~R<sup>6</sup> is a 5-6 membered saturated, partially  
saturated or unsaturated carbocyclic or heterocyclic ring  
system, or an 8-10 membered saturated, partially saturated  
or unsaturated bicyclic ring system; wherein any of said  
heterocyclic ring systems contains one or more heteroatoms  
selected from O, N, S, S(O)<sub>n</sub> or N(R<sup>2</sup>); and wherein any of~~



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said ring systems optionally contains 1 to 4 substituents independently selected from -OH, -C<sub>1</sub>-C<sub>4</sub> alkyl, -O-(C<sub>1</sub>-C<sub>4</sub> alkyl) or -O-C(O)-(C<sub>1</sub>-C<sub>4</sub> alkyl).

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2. (Amended) The compound according to claim 1, wherein R<sup>8</sup> is -C<sub>1</sub>-C<sub>4</sub>-branched or straight chain alkyl, wherein one to two carbon atoms in said alkyl are independently replaced by W, wherein R<sup>8</sup> is additionally and optionally substituted with one or more groups independently selected from -OH; -C<sub>1</sub>-C<sub>4</sub>-alkoxy; -Ht'; -O-Ht'; -NR<sup>2</sup>-CO-N(R<sup>2</sup>)<sub>2</sub>; -CO-N(R<sup>2</sup>)<sub>2</sub>; -R<sup>1</sup>-C<sub>2</sub>-C<sub>6</sub> alkenyl, which is optionally substituted with one or more groups independently selected from hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, -Ht', -O-Ht', -NR<sup>2</sup>-CO-N(R<sup>2</sup>)<sub>2</sub> or -CO-N(R<sup>2</sup>)<sub>2</sub>; or R<sup>7</sup>; and

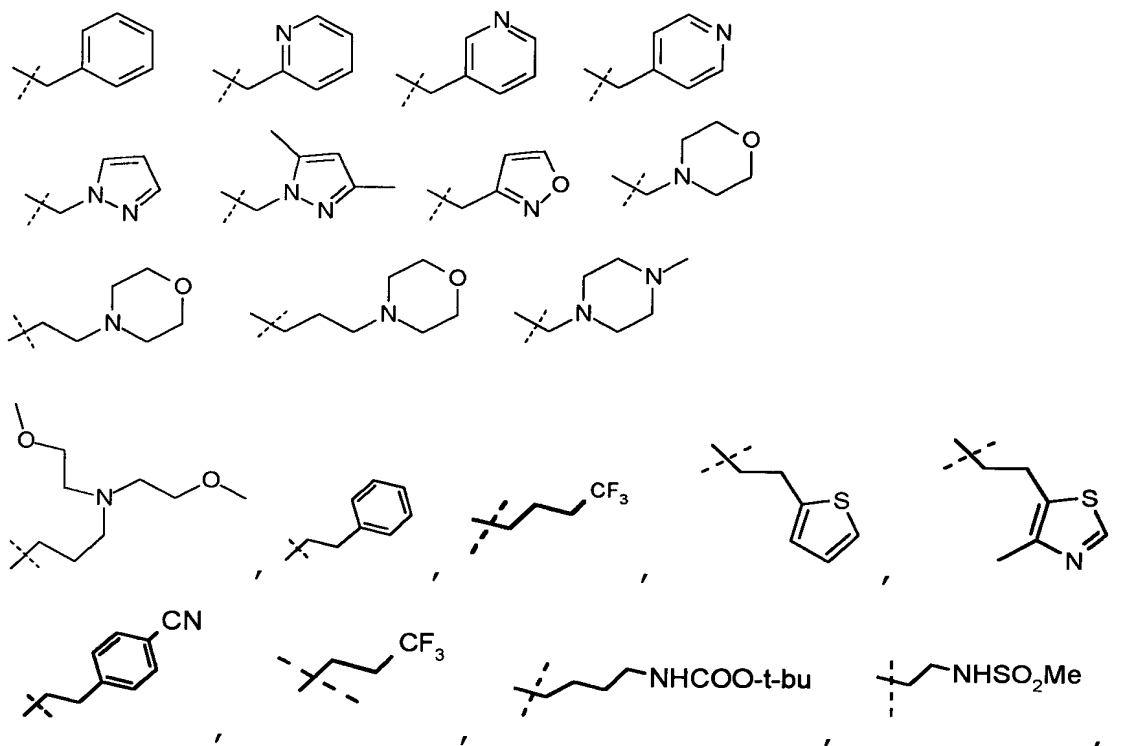
wherein W is -O-, -NR<sup>2</sup>-, -NR<sup>2</sup>-S(O)<sub>2</sub>-, -NR<sup>2</sup>-C(O)O-, -O-C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-C(S)NR<sup>2</sup>-, -NR<sup>2</sup>C(O)-, -C(=NR<sup>2</sup>)-, -C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-C(=N-CN)-NR<sup>2</sup>-, -NR<sup>2</sup>C(=N-CN)O- or -C(O)O-.

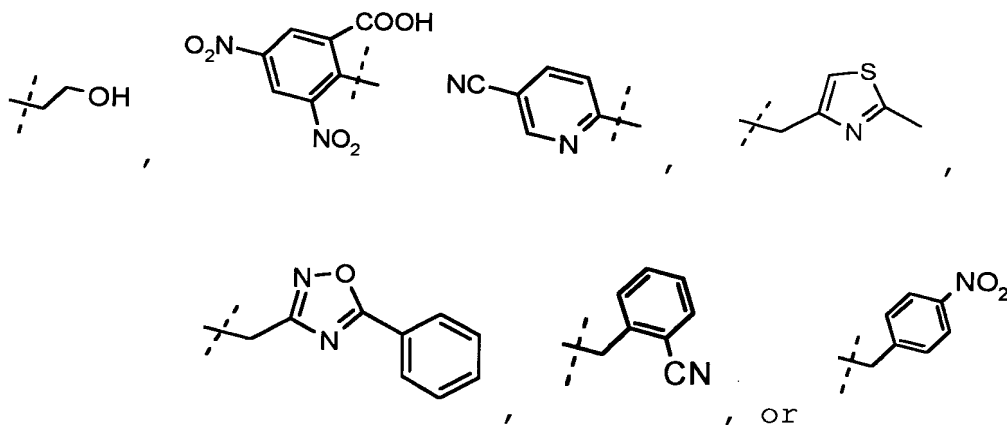
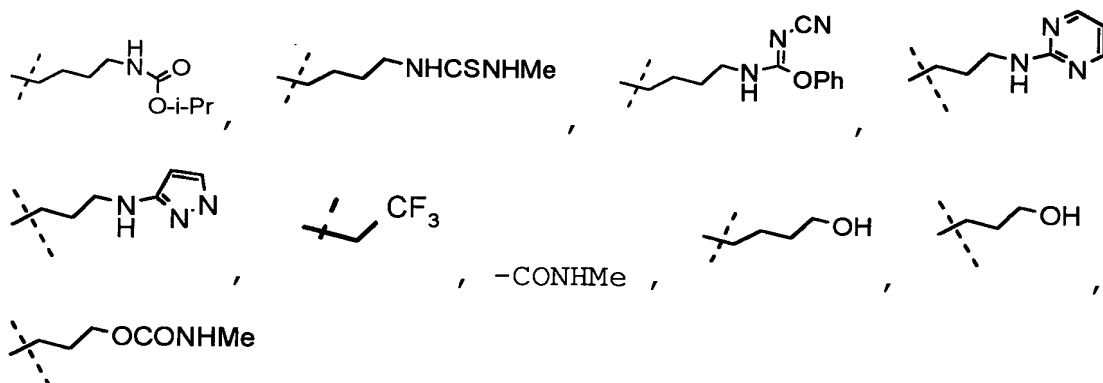
3. (Amended) The compound according to claim 1, wherein R<sup>8</sup> is a -C<sub>1</sub>-C<sub>4</sub>-branched or straight alkyl chain, wherein one to two carbon atoms are substituted with Ht';

wherein Ht' is C<sub>6-14</sub> aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more

heteroatoms selected from N, N(R<sup>2</sup>), O, S and S(O)<sub>n</sub>, wherein  
 any member of Ht' is optionally substituted with one or more  
 substituents independently selected from oxo, -OR<sup>2</sup>, SR<sup>2</sup>, -R<sup>2</sup>,  
 -N(R<sup>2</sup>)(R<sup>2</sup>), -R<sup>2</sup>-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>,  
 -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -N(R<sup>2</sup>)-C(O)O-R<sup>2</sup>, -C(O)-R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>,  
 -S(O)<sub>n</sub>-Q', methylenedioxy, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, -NO<sub>2</sub>,  
 Q', -OQ', -OR<sup>7</sup>, -SR<sup>7</sup>, -R<sup>7</sup>, -N(R<sup>2</sup>)(R<sup>7</sup>) or -N(R<sup>7</sup>)<sub>2</sub>.

4. (Amended) The compound according to claim 1,  
 wherein R<sup>8</sup> is selected from:





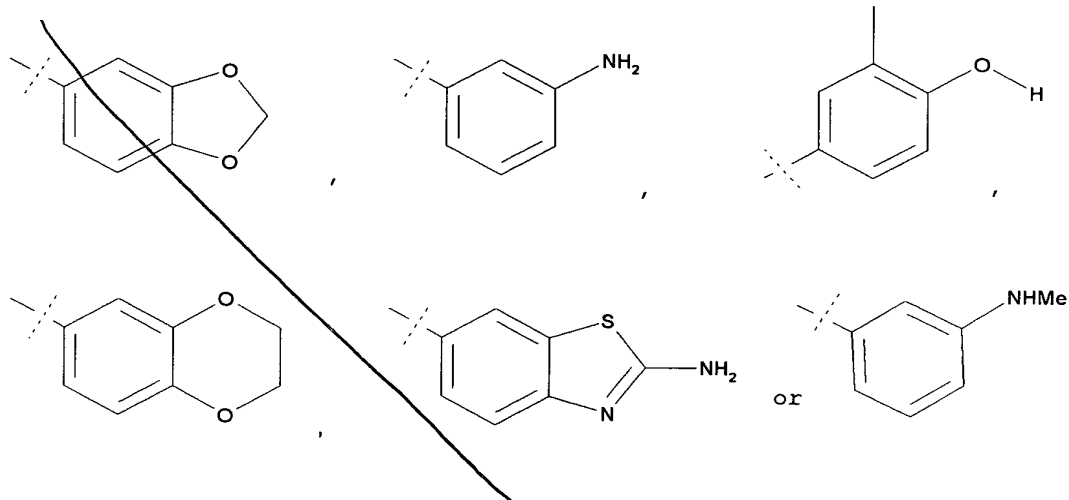
AB

wherein.

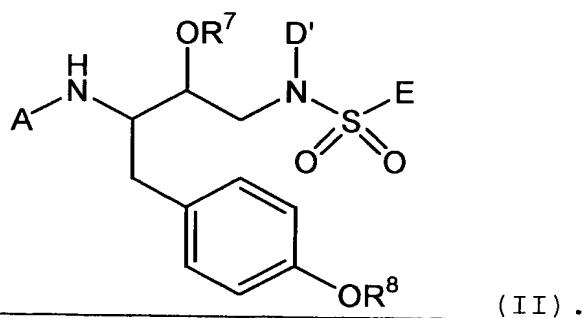
8. (Amended) The compound according to claim 1,

E is selected from:

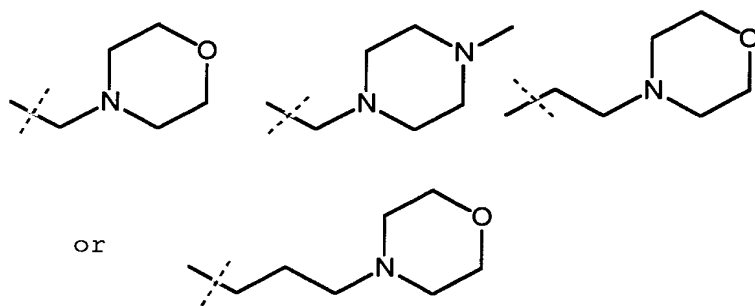
A3  
cont



9. (Amended) The compound according to claim 1, having the formula (II):

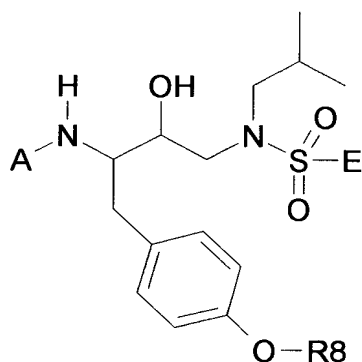


11. (Amended) The compound according to claim 9, wherein  $\text{R}^8$  is selected from:



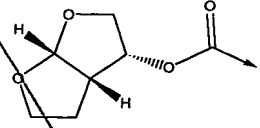
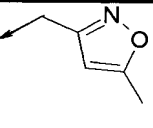
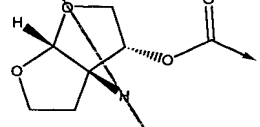
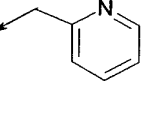
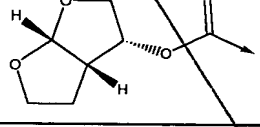
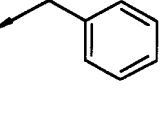
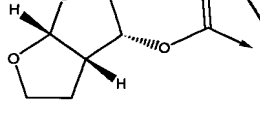
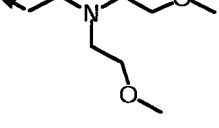
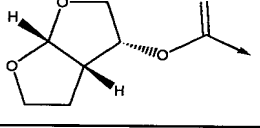
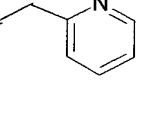
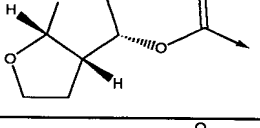
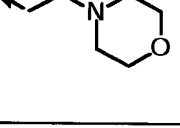
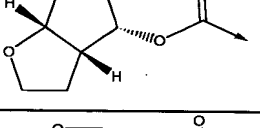
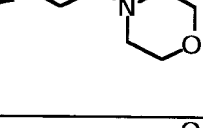
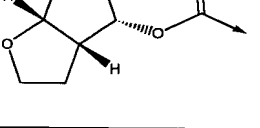
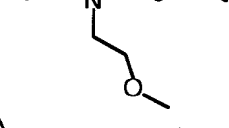
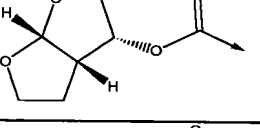
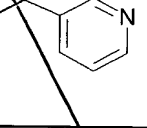
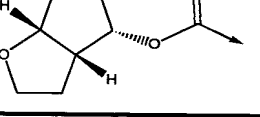
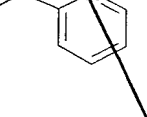
A5

15. (Amended) The compound according to claim 9, wherein said compound is selected from compound numbers: 26, 27, 31, 33, 35, 36, 38, 41, 43, 48, 49, 51, 52, 53, 54, 55, 56, 57, 59, 60, 71, 72, 73, 74, 202-204, 209, 213, 215, 217, 223, 227, 231, 233, 236, 237, 239, 243, 247, 250, 260, 263, 271, 281, 289, 293, 295, 304, 309, 317, 319, 320, 322, 334, 335, 348, 364, 367, 368, 375, 382, 383 or 396, wherein said compound is as defined below:

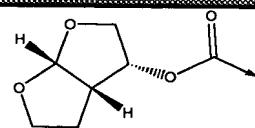
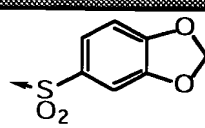
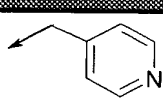
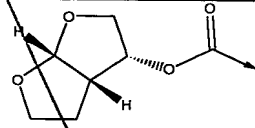
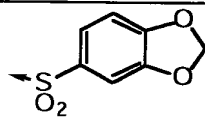
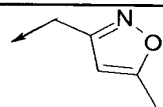
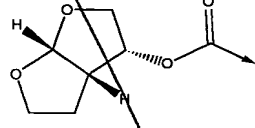
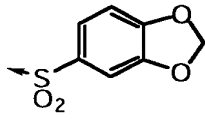
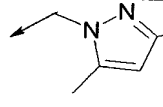
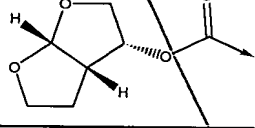
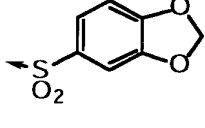
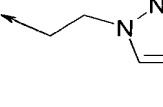
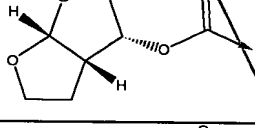
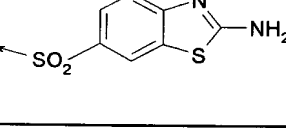
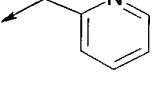
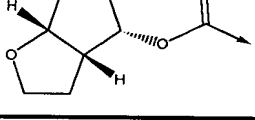
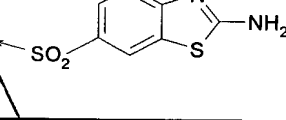
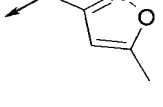


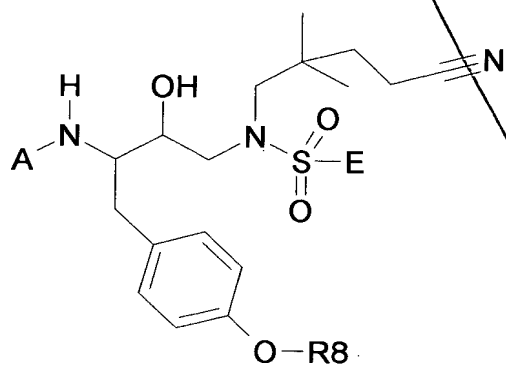
A	S(O) <sub>2</sub> E	R
26 		
27 		
31 		
33 		

AS  
cont

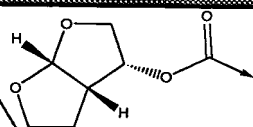
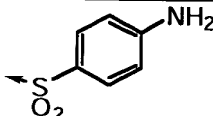
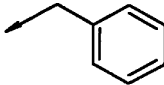
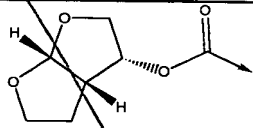
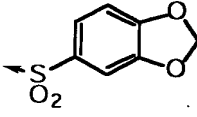
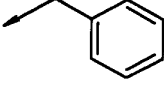
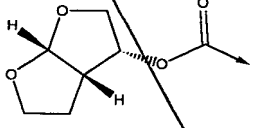
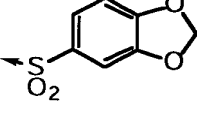
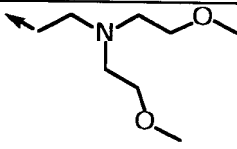
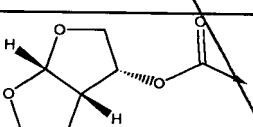
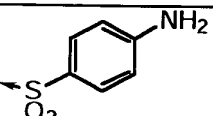
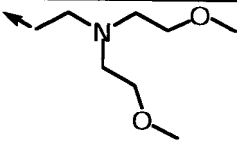
A	S O <sub>2</sub> P	R
35		
36		
38		
41		
43		
48		
49		
51		
52		
53		

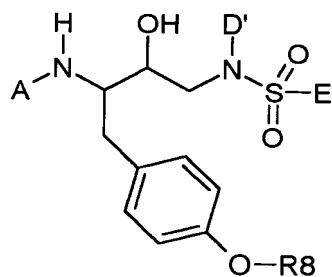
AS  
cmt

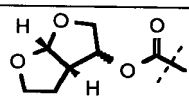
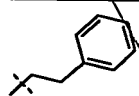
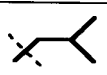
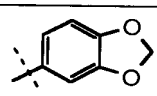
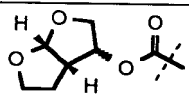
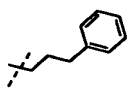
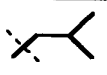
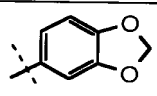
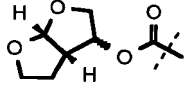
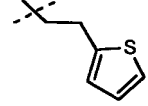
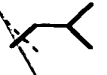
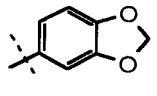
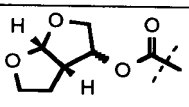
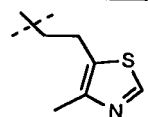
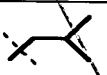
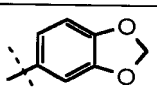
A	B	C
54 		
55 		
56 		
57 		
59 		
60 		



AS  
cont

	A	S(O) <sub>2</sub> R	R <sup>8</sup>
71			
72			
73			
74			



	A	R <sup>8</sup>	D'	E
202				
203				
209				
213				



AS  
cont

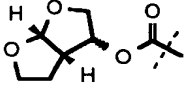
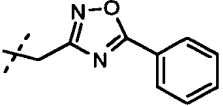

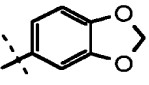
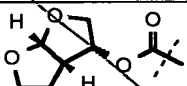


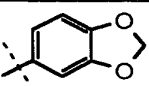
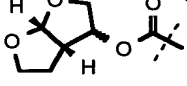
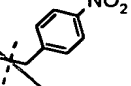

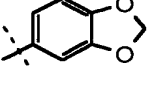
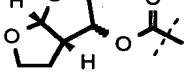
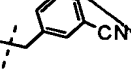
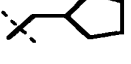
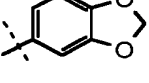
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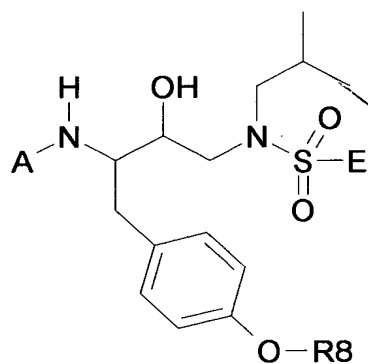
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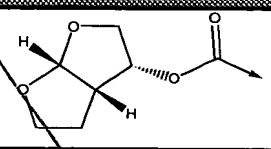
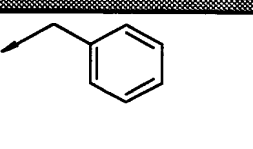
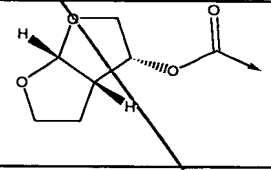
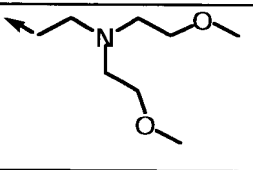
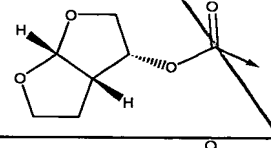
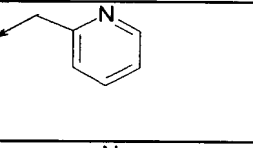
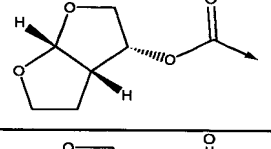
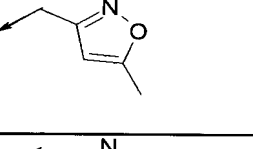
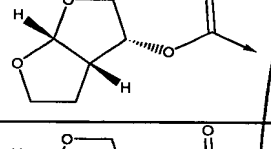
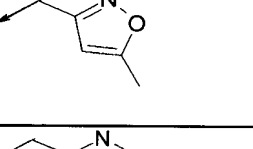
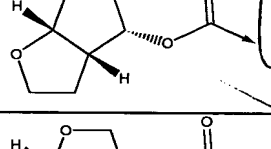
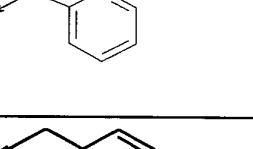
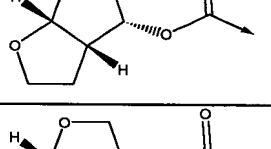
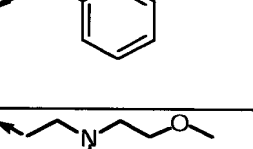
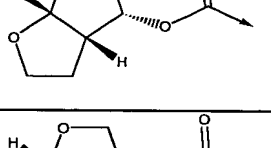
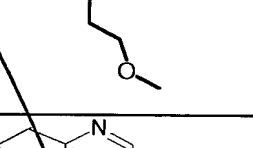
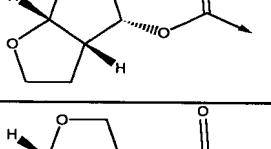
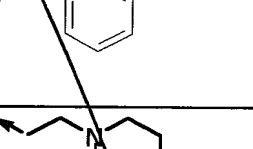
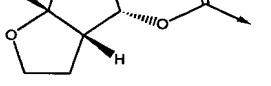
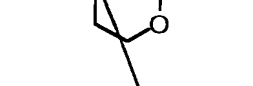
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375				
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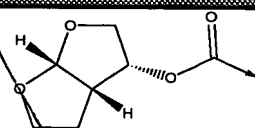
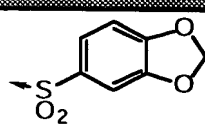
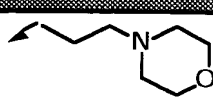
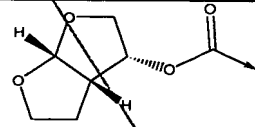
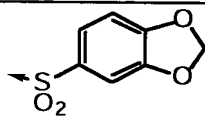
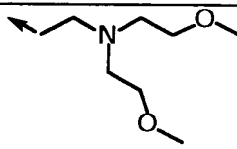
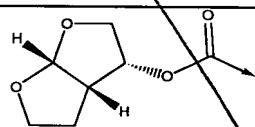
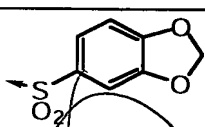
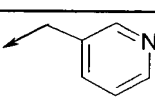
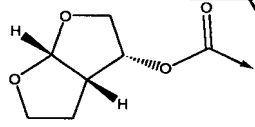
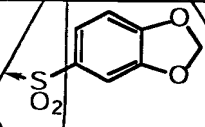
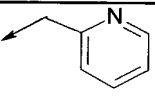
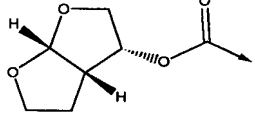
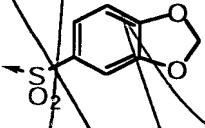
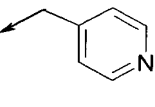
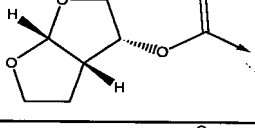
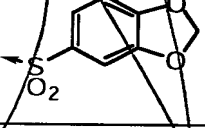
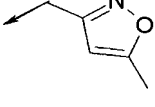
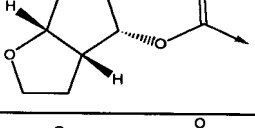
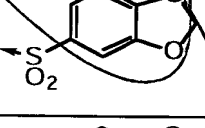
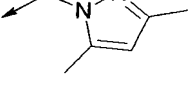
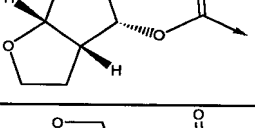
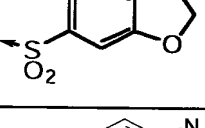
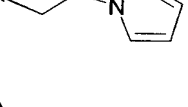
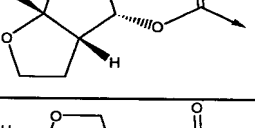
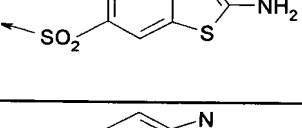
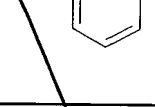
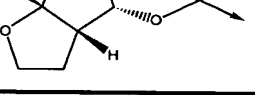
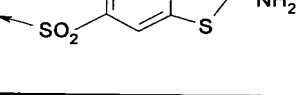

16. (Amended) The compound according to claim 15, wherein said compound is selected from compound numbers: 26, 27, 31, 33, 35, 36, 38, 41, 43, 48, 49, 51, 52, 53, 54, 55, 56, 57, 59, 60, 71, 72, 73, 74, 209, 215, 227, 233, 237, 281, 289, 295, 304, 309, 322, 335, 364, 368, 382 or 383, wherein said compound is as defined below:

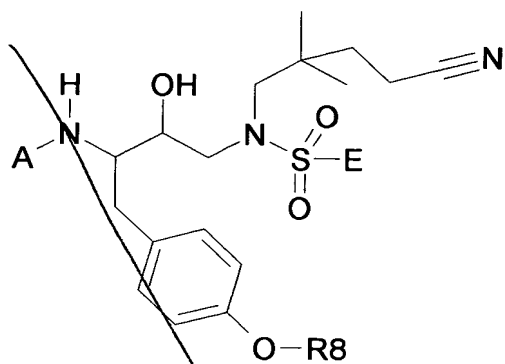


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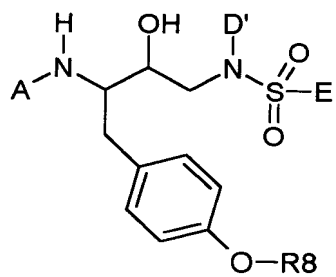
AS  
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A	S O <sub>2</sub> E	R
49 		
51 		
52 		
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54 		
55 		
56 		
57 		
59 		
60 		



AS  
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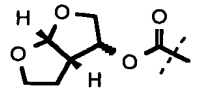
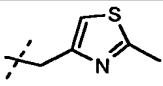

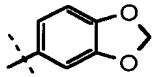
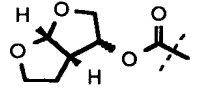
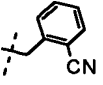

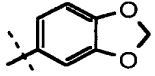
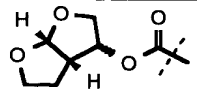
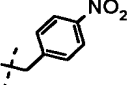

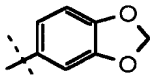
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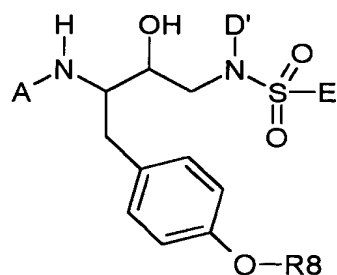
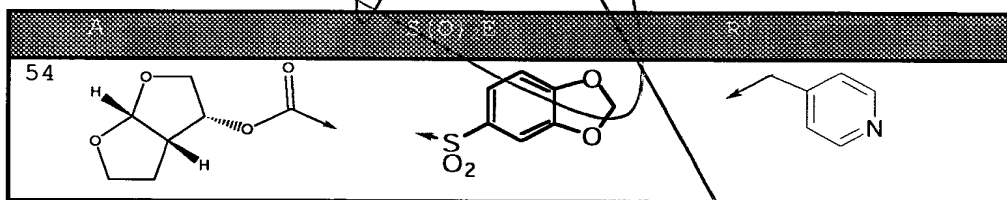
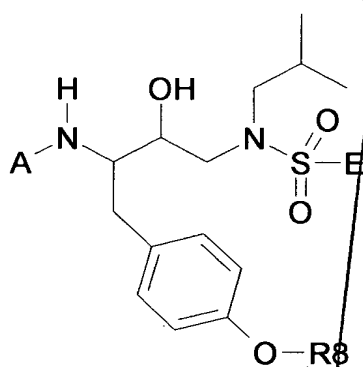
	A	R <sup>B</sup>	D'	E
209				
215				
227				
233				
237				
281				
289				
295				

	A	R <sup>B</sup>	D'	E
309				
322				
335				
364				
367				

368				
382				
383				

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17. (Amended) The compound according to claim 16, wherein said compound is selected from: 54, 209, 237, 281, 295, 309, 367 or 368, wherein said compound is as defined below:





AS and

	A	R <sup>a</sup>	D'	E
209				
237				
281				
295				

	A	R <sup>a</sup>	D'	E
309				
367				
368				
382				
383				

Sub B4 18. (Amended) A composition comprising a compound according to any one of claims 1-5 or 7-17, in an amount sufficient to inhibit an aspartyl protease; and a pharmaceutically acceptable carrier.

21. (Amended) The composition according to claim 18, wherein said composition comprises at least one additional therapeutic agent selected from (1 alpha, 2 beta, 3 alpha)-9-[2,3-bis(hydroxymethyl)cyclobutyl]- guanine [(-)BHCG, SQ-34514]; oxetanocin-G (3,4-bis-(hydroxymethyl)-2-oxetanosyl]guanine); acyclic nucleosides; acyclic nucleoside phosphonates; ribonucleotide reductase inhibitors; other 2',3'-dideoxynucleosides; other aspartyl protease inhibitors; oxathiolane nucleoside analogues; 3'-deoxy-3'-fluorothymidine; 5-chloro-2',3'-dideoxy-3'-fluorouridine; (-)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol; ribavirin; 9-[4-hydroxy-2-(hydroxymethyl)but-1-yl]-guanine (H2G); tat inhibitors; interferons; renal excretion inhibitors; nucleoside transport inhibitors; pentoxifylline; N-acetylcysteine (NAC); Procysteine;  $\alpha$ -trichosanthin; phosphonoformic acid; immunomodulators; granulocyte macrophage colony stimulating factors; erythropoetin; soluble CD<sub>4</sub> and genetically engineered derivatives thereof; non-nucleoside reverse transcriptase inhibitors (NNRTIs); 1,4-dihydro-2H-3,1-benzoxazin-2-ones NNRTIs; or quinoxaline NNRTIs.

A6  
cont

22. (Amended) The composition according to any one of claims 18-21 or 28, wherein said composition is in an orally available dosage form.

Please add claim 28 as follows:

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28. (Added) The composition according to claim 21, wherein said acyclic nucleosides are acyclovir, valaciclovir, famciclovir, ganciclovir or penciclovir; said acyclic nucleoside phosphonates are (S)-1-(3-hydroxy-2-phosphonyl-methoxypropyl)cytosine (HPMPC); said ribonucleotide reductase inhibitors are 2-acetylpyridine 5-[(2-chloroanilino)thiocarbonyl] thiocarbonohydrazone, or 3'-azido-3'-deoxythymidine; said other 2',3'-dideoxynucleosides are 2',3'-dideoxycytidine, 2',3'-dideoxyadenosine, 2',3'-dideoxyinosine, or 2',3'-didehydrothymidine; said other aspartyl protease inhibitors are indinavir, ritonavir, nelfinavir, or [3S-[3R\*(1R\*, 2S\*)]]-[3[[[(4-aminophenyl)sulfonyl](2-methylpropyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-tetrahydro-3-furanyl ester (amprenavir); said oxathiolane nucleoside analogues are (-)-cis-1-(2-hydroxymethyl)-1,3-oxathiolane 5-yl)-cytosine (lamivudine) or cis-1-(2-(hydroxymethyl)-1,3-oxathiolan-5-yl)-5-fluorocytosine (FTC); said tat inhibitors are 7-

A7  
Cmt

chloro-5-(2-pyrryl)-3H-1,4-benzodiazepin-2-(H)one (Ro5-3335)  
or 7-chloro-1,3-dihydro-5-(1H-pyrrol-2yl)-3H-1,4-  
benzodiazepin-2-amine (Ro24-7429); said interferons are  $\alpha$ -  
interferon; said renal excretion inhibitors are probenecid;  
said nucleoside transport inhibitors are dipyridamole; said  
immunomodulators are interleukin II or thymosin; said non-  
nucleoside reverse transcriptase inhibitors (NNRTIs) are  
nevirapine (BI-RG-587), loviride ( $\alpha$ -APA) or delavuridine  
(BHAP); said 1,4-dihydro-2H-3,1-benzoxazin-2-ones NNRTIs are  
(-)-6-chloro-4-cyclopropylethynyl-4-trifluoromethyl-1,4-  
dihydro-2H-3,1-benzoxazin-2-one (L-743,726 or DMP-266); or  
said quinoxaline NNRTIs are isopropyl (2S)-7-fluoro-3,4-  
dihydro-2-ethyl-3-oxo-1(2H)-quinoxalinecarboxylate  
(HBV1293).

#### REMARKS

Applicants appreciate the Examiner's telephonic discussions of the Action with applicants on August 14, 15, and 22, 2001. In particular, applicants thank the Examiner for clarifying that Amato, United States Patent 5,808,056, was listed in the Notice of References Cited only to show the state of the art.